

WHAT IS CLAIMED IS:

1. A method of adjusting the affinity of a polypeptide to a target molecule, comprising:
 - a) identifying aspartyl residues which are prone to isomerization; and
 - 5 b) substituting alternative residues and screening the resulting mutants for affinity against the target molecule.
2. The method of claim 1 wherein step b) is affinity maturation using phage display.
3. The method of claim 2 wherein the polypeptide is an antibody.
4. The method of claim 3 wherein the antibody is an anti-IgE antibody and the target molecule is IgE.
- 10 5. The method of claim 4 wherein the antibody is the sequence indicated as "E25" in Figure 12. [Seq. ID No. 13-14].
6. The method of claim 5 wherein the residues substituted are variable light chain CDR1 residues Asp32Glu, Gln27Lys and Ser28Pro.
7. The method of claim 6 wherein the additionally substituted residues are variable heavy chain CDR2
- 15 residues Thr53Lys, Asp55Ser, Ser57Glu and Asn59Lys.
8. An antibody molecule comprising an e26 sequence selected from the group consisting of: F(ab) fragment [Seq. ID Nos. 19-20], sFv fragment [Seq. ID No. 22] or F(ab)'₂ [Seq. ID Nos. 24-25].
9. An antibody molecule having a sequence which is substantially identical to the sequence "e26" of Figure 12. [Seq ID Nos. 15-16].
- 20 10. An antibody molecule comprising an e27 sequence selected from the group consisting of: F(ab) fragment, [Seq. ID Nos. 19 & 21], sFv fragment [Seq. ID No. 23] or F(ab)'₂ [Seq. ID Nos. 24 & 26].
11. An antibody molecule having a sequence which is substantially identical to the sequence "e27" of Figure 12. [Seq. ID No. 17-18].
- 25 12. An improved antibody or functional fragment thereof having improved ragweed-induced histamine release inhibition properties as a result of application of the method of claim 1.
13. An improved antibody or functional fragment thereof having improved ragweed-induced histamine release inhibition properties as a result of application of the method of claim 2.
14. A nucleic acid molecule having a sequence encoding for an e26 antibody fragment selected from the group consisting of: F(ab), sFv and F(ab)'₂.
- 30 15. A nucleic acid molecule having a sequence substantially identical to one encoding for e26.
16. A nucleic acid molecule having a sequence encoding for an e27 antibody fragment selected from the group consisting of: F(ab), sFv and F(ab)'₂.
17. A nucleic acid molecule having a sequence substantially identical to one encoding for e27.
18. A nucleic acid molecule which encodes for an antibody having improved ragweed-induced histamine
- 35 release properties as a result of the application of the method of claim 1.
19. A nucleic acid molecule which encodes for an antibody having improved ragweed-induced histamine release properties as a result of the application of the method of claim 2.
20. A composition comprising pharmaceutically-acceptable excipient(s) in admixture with an e26 antibody molecule having a sequence selected from the group consisting of: F(ab) [SEQ ID NO. 19-20]; sFv [SEQ ID NO. 22] and F(ab)'₂ [SEQ ID NO 24-25].

21. A composition comprising pharmaceutically-acceptable excipient(s) in admixture with an antibody having a sequence substantially similar to "e26" of Figure 12. [SEQ ID NO 15-16].

22. A composition comprising pharmaceutically-acceptable excipient(s) in admixture with an e27 antibody molecule having a sequence selected from the group consisting of: F(ab) [SEQ ID NO19 & 20]; sFv [SEQ ID NO 23] and F(ab)'₂ [SEQ ID NO 24 & 26].

5 23. A composition comprising pharmaceutically-acceptable excipient(s) in admixture with an antibody molecule having a sequence substantially similar to "e27" of Figure 12 [SEQ ID NO 17-18].

24. A method of reducing or preventing the IgE mediated production of histamine in a mammal comprising the administration of a therapeutically effective amount of an e26 antibody having a sequence selected from the group consisting of: F(ab) [SEQ ID NO 19-20]; sFv [SEQ ID NO 22] and F(ab)'₂ [SEQ ID NO 24-25].

10 25. A method of reducing or preventing the IgE mediated production of histamine in a mammal comprising the administration of a therapeutically effective amount of an antibody having a sequence substantially similar to "e26" of Figure 12 [SEQ ID NO 15-16].

15 26. A method of reducing or preventing the IgE mediated production of histamine in a mammal comprising the administration of a therapeutically effective amount of an e27 antibody having a sequence selected from the group consisting of: [SEQ ID NO 15-16].

27. A method of reducing or preventing the IgE mediated production of histamine in a mammal comprising the administration of a therapeutically effective amount of an antibody having a sequence substantially similar to "e27" of Figure 12. [SEQ ID NO 17-18].

20 28. A method of treating a disorder mediated by IgE comprising the administration to a mammal in need thereof a therapeutically effective amount of e26 antibody sequence fragment selected from the group consisting of: F(ab) [SEQ ID NO 19-20]; sFv [SEQ ID NO 22] and F(ab)'₂ [SEQ ID NO 24-25].

29. A method of treating a disorder mediated by IgE comprising the administration to a mammal in need thereof a therapeutically effective amount of an antibody having a sequence substantially similar to "e26" of Figure 12 [SEQ ID NO 15-16].

25 30. A method of treating a disorder mediated by IgE comprising the administration to a mammal in need thereof a therapeutically effective amount of e27 antibody molecule having a sequence fragment selected from the group consisting of: [SEQ ID NO 15-16].

30 31. A method of treating a disorder mediated by IgE comprising the administration to a mammal in need thereof a therapeutically effective amount of antibody molecule having a sequence substantially similar to "e27" of Figure 12. [Seq. ID No.17-18].